UNOFFICIAL TRANSCRIPT[1]
WASHINGTON STATE PHARMACY AND THERAPEUTICS COMMITTEE MEETING

December 15, 2004
Radisson Hotel SeaTac
8:00am – 2:30pm

Committee Attendance:

Daniel Lessler, M.D. (Chair)
Robert Bray, M.D.
T. Vyn Reese, M.D.
Angelo Ballasiotes, Pharm.D.
Alvin Goo, Pharm.D.
Jason Iltz, Pharm.D.
Janet Kelly, Pharm.D.
Patti Varley, ARNP

Committee Absence:
John White, Pharm.D.
Carol Cordy, M.D. (Vice Chair)

Quorum was shown for all Pharmacy & Therapeutics Committee motions, 2nd's, and votes.

9:00 a.m. - Committee came to order.

Announcements

- Daniel Lessler, M.D., begins with introductions of the committee and workgroup.
- Jeff Graham, M.D., consultant to the Prescription Drug Program, welcomes TVW, informs the committee members, workgroup and stakeholders that the meeting will be televised, and instructs everyone that they must be sure to speak into the microphone and to identify themselves before speaking.
- Dr. Graham announces the change in the procedure for the meeting minutes. The official minutes will be the actual audiotapes of the meetings. Unofficial transcripts of the tapes will be posted to the website for reference. This will speed up the posting of information and eliminate the need for committee approval. The DUR portion of the meeting will be in the form of minutes, however, and not transcriptions. A report of the Prescription Drug Program is being prepared and will be submitted to the governor and legislator on January 1. That may go on the website as well; also on website will be 2005 schedule.
- Dr. Lessler reminds the stakeholders that during the stakeholder input portions of the meetings all comments should be limited to 3 minutes. However, if a stakeholder would like to comment on more than one drug, that stakeholder will be allowed three minutes per drug within a class.
- Dr. Graham introduces Dr. Lawrence Martin, a physician at the VA system and Dick Mioshi, PharmD. at Harborview who works with the physicians at the mental health unit.
- Duane Thurman explains that the process of approving the minutes was causing a three-month delay in the posting of the minutes to the website. The taped proceedings, the actual tapes as provided for in the plan of operations, will be the official record and may be requested through public information request and the transcript, which will be called an unofficial transcript, is a literal transcript of the tape and this will be put on the website making it available immediately. Any questions regarding the transcripts can be answered by obtaining the actual tapes.

[1] For copies of the official audio taped record of this meeting, please contact Erika Clayton at PDP (206)521-2027 pdp@hca.wa.gov.

Beta Adrenergic Blockers

Update of Drug Class Review

- × Mark Helfand, M.D., of the Oregon Health and Sciences University is unable to attend the conference via phone at this time. Dr. Lessler presents the slide review from OHSU to the committee.
- × Dr. Lessler announces that Dr. Helfand will be available for comment later in the discussion. He also suggests that the committee approach the Beta Blocker drug class in regards to specific indication and, as Dr. Helfand might be needed for the discussion on Congestive Heart Failure, the committee might consider beginning with the indication for Migraine Headaches.
- × Dr. Lessler then reads the last motion made for Beta Blockers from the Drug Review History tab in the distributed materials. Robert Bray, M.D., made the motion the year before.
- × T. Vyn Reese, M.D., comments that pindolol was found to be ineffective in the review and should be stricken from the record.
- × Dr. Lessler agrees that there was not evidence to support it in the indication of Migraine Headaches.
- × Jason Iltz, PharmD, comments that pindolol is a Beta Blocker with ISA and that experts do not recommend that they be prescribed or used and asks if the committee should be required to strike any Beta Blocker with ISA in general or if decisions should be made according to each case.
- × Dr. Lessler suggests the committee make their decision according to the effectiveness and efficacy of each agent.
- × Dr. Bray clarifies that the comment about avoiding the use of ISA Beta Blockers was specifically for the indication of angina.
- × Dr. Lessler reiterates that the committee's recommendations would be specific to each indication.

Migraine Headaches

- × Dr. Lessler suggests that, as there were so many indications last time after the discussion, he will ask for stakeholder input. He then requests comments from the committee.
- × Dr. Bray attempts a motion.
- × Dr. Reese seconds the motion.
- × Dr. Iltz comments that the committee may want to distinguish metoprolol being both immediate and extended release.
- × Dr. Bray accepts this suggestion as a friendly amendment.
- × Dr. Lessler then reads the motion.

Motion: [Dr. Bray] after considering the evidence of safety, efficacy and special populations for the treatment of migraine headache, I move that propranolol, atenolol, metoprolol succinate, metoprolol tartrate, bisoprolol, and timolol are safe and effective. No single Beta Blocker is associated with fewer adverse events in special populations. The listed agents can be subject to therapeutic interchange in the Washington preferred drug list for migraine headache.
2nded: Dr. Reese
Vote: All in favor, motion passes

Congestive Heart Failure

- × Dr. Lessler then greets Dr. Helfand who has joined the meeting via conference phone. He suggests that Dr. Helfand answer some questions that the committee may have on the indications for Congestive Heart Failure and Post-MI.
- × Dr. Helfand requests that the last motion regarding heart failure be read.
- × Dr. Lessler then reads the last motion made for this indication : Bisoprolol, Carvedilol, and Metoprolol ER are shown to be equal in safety and efficacy in treatment for the indication of Congestive Heart Failure.
- × Dr. Lessler requests that Dr. Helfand explain the use of long acting metoprolol versus carvedilol for the indication of Congestive Heart Failure, specifically in the instance of post-hoc analysis as opposed to prospective analysis.
- × Dr. Helfand explains that all post-hoc analyses are neither invalid nor are they all the same. A general concern of post-hoc analyses is that it asks certain questions of a study or trial for which the study or trial was not designed. These concerns, however, do not apply to subgroup analysis of Merit-HF because this study was designed to answer the questions asked. More to the point, these sorts of general concerns should not be a factor for this subgroup analysis as they could have been built into the initial study, although it was

added years after and it is fair quality evidence. He then added that the merit investigators did their best to find characteristics in their data set that would replicate the Copernicus study, however, there is no way to tell if the patients in the subgroup are similar to the patients in Copernicus. It is difficult to go from an HI New York Heart Association class to Ejection Fraction groups due to overlap. Copernicus did not provide information that could be used to replicate the study precisely. This was an attempt to approximate a high-risk group as best they could be using different criteria than what was being used in the Copernicus study.

× Dr. Reese asks for clarification regarding FDA approval of carvedilol for severe heart failure with left ventricular ejection fraction less than twenty-five percent.

× Dr. Helfand confirms that this carvedilol does have FDA approval for this indication and adds that though he could not predict the decisions of the FDA he feels there is no doubt that they would rely on a study like Copernicus rather than the subgroup analyses of Merit –HF.

× Dr. Lessler asks for Dr. Helfand's comment on the fact there was a significant group from Europe included in the Merit study that showed the largest benefit in terms of mortality, which seemed to imply that the type of treatment depended on whether the patient was being treated for failure in the United States or in Europe.

× Dr. Helfand answers explaining that the effect of therapies surrounding the Beta Blocker therapy may have differed from country to country despite having identical inclusion criteria. In the United States, the mortality ratio between those treated with metoprolol and those given the placebo were indistinguishable while in Europe the mortality rate was lessened by nearly fifty percent. The Merit study raises two interpretations of this outcome; either the surrounding therapy being dispensed in Europe was compatible with the Beta Blocker therapy or whatever surrounding therapies being dispensed in the United States were not compatible with the mortality reduction from metoprolol. And so although the inclusion criteria was the same across continents, it resulted in a higher risk group in Europe than in the United States and that may be why a larger benefit was shown in this group. The third interpretation would be that it was simply a chance finding in the subgroup analysis, though this is less likely than the first two interpretations. With respect to the Copernicus study, Dr. Helfand explains that because of a group of studies known, as the Carvedilol Trials, there was, no doubt that carvedilol would reduce mortality in U.S. populations. Eighty percent of the patients in Copernicus were from countries other than the United States and the benefits were higher than those of U.S. patients. It was not statistically different but there was a reasonably clear trend showing a correlation between the developed state of the country and the effectiveness of the drug. Russia and Poland recruited the most patients and had the largest mortality reductions, somewhere around 60% as opposed to the U.S., whose mortality reductions were closer to 20%. This raises more concerns about metoprolol than it does about carvedilol but this has to do with the applicability to the U.S. population and as there is less to rely on from metoprolol (muffled speech) really Merit-HF and if it is not applicable to the U.S. there is no good evidence on long acting metoprolol. Merit HF did show a mortality reduction overall and carvedilol offers a more direct route than short acting metoprolol.

× Andre Rossi, PharmD, Pharmacy Director for the Department of Corrections, asks Dr. Helfand if any specific condition played a major role in tolerating carvedilol versus metoprolol, specifically at the initiation of the therapy.

× Dr. Helfand explains that it was difficult to make a judgment as the group of patients had already been tested for tolerability before the initiation of the trial, and anyone who could not tolerate even small amounts of the drug was excluded from the randomization.

× Dr. Lessler asks the committee if there are questions regarding Beta Blockers for the indication of Post-MI ejection fracture less than 40%, which is where the data and information become more complicated.

× Dr. Reese asks if carvedilol was the only drug that has been studied with recent MI and LV dysfunction in combination with Ace Inhibitors; he adds that there seems to be a deficiency of knowledge regarding how other Beta Blockers might react in this circumstance.

× Dr. Helfand explains that the studies for carvedilol were done by recruiting stable inpatients with recent MI and asymptomatic LV dysfunction as opposed to older Beta Blocker studies that were conducted before they tried to divide people into subgroups. It would be pointless to conduct trials with similar drugs because we already know that all patients with recent MI will benefit from the addition of Beta Blockers. Several studies conducted in the late nineties are subgroup analyses of many of the previous trials that examined the subgroups of trials that recorded LV function. The subgroup within that had poor LV function. This was considered fair evidence and would suggest that other Beta Blockers were effective across subgroups. Dr, Helfand suggests that this would indicate a benefit in both normal LV function groups and the subgroup with lower ejection fractions. Capricorn, like Merit HF, had a problem with where it was done; they had a problem recruiting patients in North America where people apparently said the case of beta blockers in all patients with MI had already been proven so there was no reason to randomize a patient. The trial did not successfully recruit in North America because the previous trials did not divide the subjects in to many small categories, they just said recent MI worked well enough to tolerate a beta blocker randomizer with the

placebo or treatment and shows that they all benefit. The ledger is on the use of ace inhibitors, thrombolytics and angioplasties. Capricorn was clearly done in a more modern era, observational studies in the modern era do not suggest any difference between carvedilol and other drugs. Post hoc subgroup analyses in a meta-analysis setting of several of previous trials that had not supported subgroups but had available data on LV dysfunction supported the idea that the others are effective across a range of LV function and patients with recent MI.

× Dr. Lessler opens the floor for stakeholder comments on the indication of failure and low injection fracture of Post-MI and then introduces David Beeman from AstraZeneca.

× Dr. Graham requests that any materials regarding medication that will be commented upon should be submitted to the OHSU prior to the committee meetings.

× Dave Beeman, Medical Information Scientist for AstraZeneca, states that Toprol XL is the most prescribed medication by cardiologists for this indication. The reasons for this, he explains, go beyond the FDA indications. Toprol XL provides once daily dosing and a consistency of blood concentration over a twenty-four hour period. Additionally, because the most frequent cause of death in heart failure is sudden death from arrhythmias, he feels that it is important to have a once daily product available that is not subject to the peak and drop fluctuations over a twenty-four hour period.

× Neal Perlmutter, M.D., a cardiologist from Overlake Hospital, in Bellevue, explains that he has been involved in heart failure quality improvement projects since 1989. He encourages the use of carvedilol for improving heart function as carvedilol has lessened the number of people who suffer from myocardial infarction. As a DSHS endorsing prescribers, he and his colleagues, use carvedilol for heart failure and for high-risk patients after myocardial infarction as an inclusive agent. He agrees with the speaker from AstraZeneca who stated that Toprol XL was the most commonly used Beta Blocker and that its use goes beyond that as an agent to lessen heart failure and high risk myocardial infarction. Toprol XL is also used for angina rate control, atrial fibrillation and for super ventricular arrhythmias for these two specific indications and its use is still very important in his practice. Under the DSHS prescribing system much of the clinic's work must be done twice when carvedilol is not available on the formulary. This drug is available on every other commercial formulary in the state. He explained that he and his colleagues work to titrate their patient's medical therapy carefully, often with immigrant patients who speak limited English and find it difficult to get prescriptions filled at pharmacies or encounter confusion with doctors. He approached the subject of the Karma trial explaining that many people view this as a head-to-head trial although that was not its intent. It was set up to answer one of two questions; is beta one blockade the answer or are there mechanisms beyond beta one blockade that carvedilol has that can result in extra benefits? Those involved in the Karma trial were meticulous in achieving equal levels of beta one blockade in short-acting metoprolol versus carvedilol. The results seem to suggest that the mechanisms for this additional benefit are something beyond selective beta one blockade. There have been some concerns in respect to the fact that they did not use 200mg of Toprol XL in the trial. If everyone were to use that dose in practice, equal results would be achieved. In fact, that dose is only used 6 percent of the time in clinical practices as it is tolerated so poorly. He concludes by stating that carvedilol should be included on the formulary.

× Dr. Graham requests that those stakeholders speaking identify whether or not they are sponsored and who sponsors them.

× Dr. Long Nguyen, Medical Scientist, from GlaxoSmithKline, comments that the post-MI with LVD carvedilol has been shown to increase mortality and this mortality benefit is in addition to patients who already receive ace inhibitors, this why there is not much mortality benefit in Europe versus the United States because the quality of care in the United States is much higher than it is in Europe and other countries. It is known that the majority of patients will benefit from ace inhibitors and of which dosage they will benefit from versus other patients from other countries. Additionally, carvedilol is the only beta blocker with the FDA approval for post-MI LVD and severe heart failure, clearly indicating carvedilol has enough robust data available for FDA to approve for these patients in terms of safety and efficacy and he recommends that the board consider adding and expediting prior authorization for Coreg or carvedilol for patients in treatment for both mild to severe heart failure as well as patients with post-MI and LVD treatment.

× An Pham, PharmD, Medical Science Liaison with Reliant Pharmaceuticals, Inc. InnoPran XL is an innovative formulation of propranolol HCL following the landmark results of BHAT (Beta Blocker Heart Attack Trial) data in which propranolol was associated with significant reduction in the morning peak incidence of sudden cardiac death compared to placebo and a statistically significantly larger reduction in mortality in patients with recent heart attack or post-MI. To accomplish this, InnoPran XL employs Eurand Diffucaps™, a delayed-onset, controlled-release technology that produces a chronotherapeutic formulation of propranolol hydrochloride. The capsules contain sustained-release beads, each of which contain propranolol hydrochloride and are coated with dual membranes. More importantly, InnoPran XL provides

24-hour blood pressure and heart rate control. Presently, InnoPran XL is indicated for the management of hypertension to be taken at approximately 10PM or bedtime. There is no generic equivalence available for long acting propranolol for either Inderal LA or InnoPran XL. Propranolol has demonstrated clinical benefit in other conditions including tremor, migraine prophylaxis or prevention, recent heart attack or post-MI, and chronic stable angina. In addition, InnoPran XL is currently on PDL in Idaho, Texas, and other states across the country. Even though the drug has only recently being introduced to the physicians in Washington, the usage has increased suggesting that physicians here also find that this formulation has distinct advantage for the care of hypertensive patients with high risk for cardiac events. In summary, Dr. Pham strongly asks the P&T Committee to recommend InnoPran XL to be on Washington State Preferred Drug List or formulary for the following benefit considerations: chronotherapeutic approach on hypertension treatment with PM dose and AM peak effect, Important therapeutic benefit for patients to decrease morbidity and mortality from morning cardiovascular events, and safety and tolerability with low incidence of side-effects

Committee Deliberation and Vote

- Dr. Lessler opens a discussion and requests that Dr. Reese read the motion he made the year before on Beta Blockers for the indication of Congestive Heart Failure.
- Dr. Reese reads the motion: Bisoprolol, Carvedilol, and Metoprolol ER are shown to be equal in safety and efficacy in treatment for the indication of Congestive Heart Failure.
- Dr. Bray voices concern in regards to motion crafting and the use of the term “equal”. While the committee has heard strong evidence in favor of the use of carvedilol for improvement in severe heart failure, no evidence was presented indicating other drugs in the group were equally efficacious although there was evidence presented indicating that other drugs were efficacious. It almost appears that the Class 4 heart failure patient is a special population and though can safely be stated that those same drugs are efficacious, a comment may need to be made allowing carvedilol to be available to those patients who have Class 4 heart failure.
- Dr. Reese agrees and states that he believes 2 motions should be made for that group, one for severe heart failure with ejection fracture less than 25% and one for heart failure with ejection fracture greater than 25 %.
- Alvin Goo, PharmD, agrees with Dr. Bray and Dr. Reese and asks if MAA is able to manage the differentiation of ejection fractures greater or less than 25%.
- Dr. Lessler directs this question to Siri Childs, PharmD., Pharmacy Policy Manager for MAA - DSHS and Jeff Thompson, M.D. Director of MAA - DSHS.
- Dr. Thompson explains that MAA would be capable of making the distinction in different ejection fractures if the motion were to include some type of clinical indications that could be applied for expedited prior authorization or prior authorization.
- Dr. Childs adds that the responsibility of coding the EPA would be that of the pharmacists who would then need to contact the prescriber that would be unfortunate if the prescriber were an endorsing practitioner. The pharmacist would need that information from the prescriber, as the patient will most likely not have that information.
- Dr. Reese interjects that he would prefer to avoid a situation in which someone with an injection fraction less than 25% were stabilized on carvedilol and then had their medication therapeutically interchanged with another drug.
- Dr. Thompson explains that the endorsing providers can write DAW on the prescriptions and bypass the therapeutic interchange of the non-preferred drugs. It is possible to coordinate care with Prior Authorization or EPA as there is not clinical data within the claims systems, if issues do arise, the cardiologist, primary care and the observation at the pharmacy level will deal with them.
- Dr. Childs suggests that if the motion included language noting the patient’s history of heart failure it would allow the pharmacist to proceed with Coreg specifically as this was the procedure used with Toprol.
- Dr. Reese asks Dr. Childs to clarify her statement.
- Dr. Childs replies that she does not believe that pharmacist level use of the system will determine the differentiation to the degree needed.
- Angelo Ballasiotes, PharmD, asks if the clinician can write on the prescription itself with regards to heart class or ejection fraction in order to expedite filling the prescription.
- Dr. Childs explains that while this direction can certainly be given it is likely that it will not be carried out in practice that would cause the pharmacist to call the prescriber and if that prescriber endorses the PDL they will not appreciate a call from the pharmacist.
- Dr. Bray suggests they consider all options in approaching their goal, the concern is that a motion will be interpreted differently than was intended. The goal is to make carvedilol available as an agent that will not

be substituted inadvertently. He suggests that the committee list all drugs that should be required and ask that a specific drug be available on an expedited PA by an endorsing practitioner and if the practitioner is not endorsing than the pharmacist can contact that doctor.

- Dr. Childs explains that the other option would be to insert a computer edit to identify an EPA ensuring that carvedilol would not be substituted for a preferred drug and no interchange would take place.
- Dr. Reese suggests that the safest way to construct the motion would be to include carvedilol as a preferred drug, while the other drugs are fine for less severe heart failure, carvedilol has been shown to be the only one effective in ejection fraction less than 25% .
- Dr. Goo voices his concern in regards to the Comet studies and such trials with carvedilol and high risk groups with CHF and prior history of hospitalization. He asks, if both drugs were put on the formulary, would there be a way to differentiate for the indications to make it easier for patients, providers and pharmacists.
- Dr. Lessler agrees with Dr. Goo and expresses his concern about constructing a motion that would specifically indicate a particular ejection fraction as well as concerns about interchange occurring when it would not be appropriate.
- Dr. Thompson explains that if the committee comments on the best clinical use, MAA would be able to work to ensure that the appropriate communication, whether EPA or PA criteria, is available. The broader the recommendation, the more difficult it becomes to obtain PA or EPA criteria. Dr. Thompson asks the committee for their best clinical judgment to enable MAA to construct an administrative option.
- Mark Stern, Department of Corrections, endorses the statement made by Dr. Thompson, encouraging smaller applications of this process with easier administrative controls.
- Donna Marshall, PharmD, Pharmacy Director for Uniform Medical Plan, reminds the committee and workgroup that a similar situation was presented during the last motion made for Statin drugs. The instructions were to designate atorvastatin as a high potency option and pravastatin as a lack of drug interaction and that neither were subject to interchange, other drugs were then listed as equally safe and effective and were interchangeable.
- Dr. Reese attempts to craft the motion.
- Dr. Graham suggests that the committee combine the first and second motion and list the conditions at the end of the motion.
- Discussion between committee members regarding not therapeutically interchanging carvedilol.
- Dr. Reese again reads the motion including the statement that carvedilol must be on the PDL.
- Dr. Marshall asks if the committee would like to indicate for severe CHF.
- Drs. Reese and Lessler both agree that this would be too complicated and decline the suggestion.
- Dr. Marshall requests clarification regarding the reference of metoprolol, whether Extended Release or Short Acting.
- Dr. Thompson asks for clarification regarding whether carvedilol should be on the PDL for all Beta Blocker indications or only for heart failure indication.
- Dr. Reese says that carvedilol shall only be mentioned for the congestive heart failure indication and shall not be therapeutically interchanged.
- Dr. Bray states that the committee is currently speaking of congestive heart failure only.
- Dr. Marshall reads the motion as seen on the projection screen.
- Dr. Reese announces that this is now his motion.
- Dr. Lessler asks that Dr. Marshall add in the last line about bisoprolol and metoprolol for congestive heart failure.
- Patti Varley, AARNP, expresses concern regarding the line "I move that three medications are safe effective and have no adverse events in special populations of CHF", she feels this is confusing as congestive heart failure is a special population.
- Dr. Marshall explains that although congestive heart failure that is a special population within the indication there are no sub-populations of heart failure patients showing a difference.
- Dr. Reese suggests they insert the word severe before heart failure.
- Patti Varley says that is not necessary that she understands now.
- Dr. Reese reads the formal motion:

Motion: [Reese] After considering the evidence of safety, efficacy and special populations for the treatment of congestive heart failure, I move that bisoprolol, carvedilol, and metoprolol succinate are safe and effective. No single beta blocker is associated with fewer adverse events in special populations. Carvedilol should be on the Washington PDL for heart failure patients and shall not be interchanged for the indication of heart failure. Bisoprolol and metoprolol succinate may be subject to interchange for heart failure on the Washington preferred drug list.
2nd: Dr. Iltz

Vote: All in favor, motion passes.

Hypertension

- × Dr. Lessler asks for a comment on this indication
- × Dr. Bray comments the committee has already made carvedilol available on the PDL.
- × Dr. Reese agrees that this is a moot point.
- × Dr. Lessler announces that the committee will speak of hypertension next
- × Dr. Reese reads the last motion made and then comments that there is no new evidence that any one drug is better than the other and that he will make the same motion with the new format after discussion by the committee.
- × Dr. Lessler suggests that the committee exclude the word "equally" and comment only on safety and efficacy. He also inquires as to whether or not the committee has listed those Beta Blockers that are licensed in the United States.
- × Dr. Reese states that the FDA according to his list has approved all drugs mentioned for hypertension.
- × Dr. Lessler suggests that Dr. Reese read the motion:

Motion: [Reese]After considering the evidence of safety, efficacy and special populations for the treatment of hypertension, I move that acebutolol, atenolol, betaxalol, bisoprolol, carteolol, carvedilol, labetalol, metoprolol titrate, metoprolol succinate, nadolol, penbutalol, pindolol, propranolol, propranolol ER, and timolol are safe and effective. No single beta blocker is associated with fewer adverse events in special populations. The listed drugs can be subject to therapeutic interchange in the Washington preferred drug list for the treatment of hypertension.
2nd: Dr. Goo
Vote: All in favor, motion passes.

Angina

- × Dr. Goo comments that the only change in the angina indication is the idea to exclude Beta Blockers with IS activity.
- × Dr. Lessler suggests that Dr. Goo read the motion, as he was the last committee member to make a motion for angina.
- × Dr. Goo reads the motion off the projected screen.
- × The committee members comment and tweak the language.
- × Dr. Goo reads the corrected motion.
- × Dr. Graham announces that it has been brought to his attention that the motion should read " …there are no beta blockers more effective or associated with fewer adverse effects in special populations" as there are adverse events in special populations, such as asthmatics and so forth. Dr. Graham feels the committee should follow the language of the question asked in the reports. The committee should state that there are adverse effects but there are not more in any special populations; those subgroups are defined as demographics based on age, race, gender and other medications, drug-drug interactions and co-morbidities.
- × Dr. Lessler comments that although this language was used in previous motion earlier in the day the committee can substitute this corrected language in the previous motions without changing the intent.
- × Dr. Lessler requests that Dr. Marshall add "no single beta blocker" to the motion being projected onto the screen.
- × Dr. Lessler encourages Dr. Goo to read the motion.
- × Dr. Goo then reads the motion as follows:

Motion: [Goo] after considering the evidence of safety, efficacy and special populations for the treatment of angina, I move that atenolol, bisoprolol, carvedilol, labetolol, metoprolol titrate, metoprolol succinate, propranolol, propranolol ER, and nadolol are safe and effective. No single beta blocker is associated with fewer adverse events in special populations and can be subject to therapeutic interchange in the Washington preferred drug list for the indication of angina.
2nd: Dr. Iltz

- × Dr. Reese questions labetolol's FDA approval for angina.
- × Dr. Goo presents a study from 1986 included in the report showing no difference between labetolol and atenolol.

Vote: All in favor, motion passes.

- × Duane Thurman, Senior Prescription Drug Program Manager for HCA, suggests that the committee again consider the different language used.
- × Dr. Lessler agrees and suggests that the committee consider changing the language. He wants to be sure that in substituting language around special populations that he does not specifically change what was said in the previous motions.
- × Duane Thurman comments that it would be helpful that the intent of the committee is to change the language to resemble more closely the questions being considered in the underlying evidence and not to change the intent.
- × Dr. Lessler comments that the committee wants to be sure that the intent of the motions is not altered.
- × Dr. Marshall suggests changing the previous motions made that day.
- × Duane Thurman suggests a vote to ratify the changes in the language.
- × Dr. Lessler states that the committee has made those changes in the language of previous motions to concur more specifically with the questions to OHSU. He then asks if there is a motion to accept the changes made in the language with respect to special population.
- × An unidentified committee member made the motion.
- × An unidentified committee member seconded the motion.

Atrial Arrhythmias

- × Dr. Reese comments that there will be a few more drugs that added to the motion.
- × Dr. Lessler comments that the committee will add some additional agents, and then asks if the committee members have any other changes to be made.
- × Dr. Reese reads the motion with the additional list of drugs.
- × Dr. Marshall asks Dr. Reese to be sure that she has listed all the drugs that he named.
- × Dr. Reese suggests adding propanolol, IR and LA.
- × Dr. Reese then reads the motion again:

Motion: [Reese] After considering the evidence of safety, efficacy and special populations for the treatment of Atrial Arrhythmia, I move that atenolol, nadolol, pindolol, propranolol, propranolol ER, metoprolol succinate, metoprolol tartrate, and carvedilol are safe and effective. No single beta blocker is associated with fewer adverse events in special populations. The listed drugs can be subject to therapeutic interchange in the Washington preferred drug list for Atrial arrhythmia.
2nd: Dr. Ballasiotes
Vote: All in favor, motion passes

Bleeding Esophageal Varices

- × Dr. Ballasiotes reads the last motion made for this indication.
- × Dr. Lessler requests double check on the evidence table of the drug pindolol.
- × Dr. Lessler announces that the committee will remove pindolol, as it is not listed in the evidence received at this time.
- × Dr. Goo then crafts a motion:

Motion: [Goo] after considering the evidence of safety, efficacy and special populations for the treatment of bleeding esophageal varices, I move that atenolol, nadolol, and propranolol are safe and effective. No single beta blocker is associated with fewer adverse events in special populations. The listed drugs can be subject to therapeutic interchange in the Washington preferred drug list for the indication of bleeding esophageal varices.
2nd: Dr. Bray
Vote: All in favor, motion passes

- × Dr. Lessler suggests that the committee repeat the exclusion of beta blocker post-CBG or silent eschemia thus concluding the Beta Blocker review.

2nd Generation Antidepressants

Dr. Lessler announces that if the committee has not reached a certain set of motions by the conclusion of their allotted time than the review of the 2nd Generation Antidepressants will be continued in February.

Dr. Thompson announces that MAA has been hosting a series of meetings with DSHS Aging and Mental Health and that another meeting will be held with stakeholders. The meetings have been established so that the mental health community can come together and work through 2005 to reach an agreement about the pharmacological treatment of mental health for the state of Washington. MAA will try to move the P&T recommendations and to preview OHSU's reviews prior to the P&T committee. It is MAA's hope that there will be a general agreement with the community who will then present their hopes for procedures of mental health pharmacology in the state of Washington.

Update of Drug Class Review

Dr. Reese reads presentation arranged by Dr. Richard Hansen as Dr. Helfand is unable to attend the meeting via phone.

- Dr. Lessler suggests that in terms of crafting the motion the committee should discuss each indication individually but only having one motion that covers the breadth of indications. He then introduces Dr. Larry Martin from the VA in Seattle and Dr. Dick Mioshi, from Harborview who deals exclusively with mental health medications.
- Dr. Lessler comments that the review did not offer much difference in effectiveness across multiple indications. He asks if the Dr. Martin or Dr. Mioshi can help to conceptualize a recommendation to the PDL.
- Dr. Martin comments on the review saying that he is impressed, that all the drugs were initially developed as antidepressants and then indications were extended to other illnesses, usually by a process of trial and error. He states that in general there is not a lot of information on pediatric studies for this drug class. Prozac is the only drug that has FDA indication for use in pediatrics in major depression and is not used often as is a complicated drug. He also feels that every drug has its use and that they should be available to providers. He explains that there is an approach, other than looking at an individual's needs, such as taking into consideration drugs that cross the blood-brain barrier and because of this they have a wide variety of side effects and each side effect has a different profile. Each drug is unique in its profile and the intensity of the binding that takes place as well as other factors. There are also side effects and adverse effects of the given medications, as well as patient characteristics, major depression comes in mild, moderate, and severe and some are extremely severe, the issue of severity of illness and prior experience with the drug co morbidities, age, gender, cultural background and biases. In every prescribing situation, the doctor is trying to match drug to the patient.
- At this point Dr. Helfand joins the group via conference phone.
- Dr. Martin continues to speak positively of the situation in which the doctors have a more unlimited choice of drugs, but that there is no preference of brand over generic drugs.
- Dr. Lessler summarizes Dr. Martin's statement by explaining to Dr. Helfand that he feels there is a need for flexibility in prescribing antidepressant medications.
- Dr. Ballasiotes agrees with Dr. Martin regarding a less limited choice of preferred antidepressants as he deals with them on a daily basis. He explains that every nervous system operates in a specific way and the each drug is different and so some drugs work differently with different people, with different side effects and co-morbidities. He adds that he not only works with the mentally ill but the mentally ill who are substance abusers and so the selection of medications is even more of a challenge and it is best to have a broad array of drugs available.
- Patti Varley comments that she also has had similar experiences. She notices a lack of head- to- head trials supplying sufficient information to decide that one drug is individually better than any other drug.
- Dr. Reese asks Dr. Helfand to comment on drug-drug interactions, specifically that of paroxetine and fluoxetine.
- Dr. Childs makes an inaudible comment.
- Dr. Lessler welcomes Dr. Hanson.
- Dr. Mioshi comments that family practice physicians prescribe 60-80% of 2nd Generation antidepressants and the doses were eventually made for that population. People have found the drugs to be equal and

effective, with some pluses and minuses, some drug interaction, and some side effects. He adds that with a larger array of availability there is more choice.

- × Dr. Lessler comments this is very different from any drug classes the committee has reviewed before as with other drug classes, side effect profiles and effectiveness have been almost the same but with this drug class there are other issues of pharmacological dynamics, onset, side effect profiles and matching medications to specific patients.
- × Dr. Thompson comments that this is the first drug class the committee has reviewed under 6088 with the refill amendment and that this discussion is not regarding changing a patient's current therapy but a patient's first start on mental health drugs.
- × Dr. Martin comments that in the treatment of depression the goal is to bring the patient to remission, meaning an absence of symptoms and a return to normalcy, adding that all drugs offer 60-70% response which is not the same as remission. The fewer choices of drugs available in this class the more chances there are of response and the less likely a chance of remission will be.
- × Dr. Bray asks Dr. Helfand to comment on three points. The first is in respect to the reports of the issue of inducing a manic episode in a bipolar patient with the use of some of the drugs available and the benefit of buproprion. The second is on the risk/benefit ratio of major depression in pediatrics and the evidence in age and size cut-offs. The third is regarding the benefits of the drug nethazadone.
- × Dr. Helfand responds to the idea that it is better to have a wider variety of available drugs. He presents the statistic that only 40% of people have a lack of a clinical response to a drug and the chance of having a full recovery on an antidepressant is even less than that. He explains that many people do not respond to their first treatment. The evidence that OHSU presents supports the idea but not everybody responds to the first treatment, some people respond to the second treatment only. Evidence does not support, very well that tailoring initial therapy based on patient characteristics, other than drugs that might interact and certain aspect of age, although this happens frequently in clinical practice. Doctors may also tailor therapy to an individual's therapy. For example, with buproprion the doctor can find out the worries that they patient has in regards to certain side effects. To answer the question regarding methazadone asked earlier in the meeting; our report did not come up with any unique benefit of methazadone. In regards to the questions of pediatrics asked earlier in the meeting, the evidence in children is meager for most of the drugs and its better for fluoxetine.
- × Dr. Mioshi comments that when patients complain of sexual side effects and want to discontinue their medication there are only a few drugs within this group from which to choose, nefazadone and buproprion. Mirtazapine is a plus/minus, as the data did not present well for this drug due to the high dropout rate. He then addresses the question regarding determining pediatric and age cut-offs and explains that there are no good answers, possibly the brain, possibly weight.
- × Dr. Helfand agrees with Dr. Mioshi as he also finds patients expressing preferences not only in respect to sexual side effects, but to weight gain side effects as well. The evidence presents identical rates of dropouts for both drugs, what is missing from the study are television advertisements and the word of mouth reputation of the drugs studied.
- × Dr. Martin comments with respect to nefazadone, explaining that many practitioners who have gone through several drugs and found nefazadone most useful, it is difficult to tell which drug will prove most efficacious for which patient. Liver toxicity associated with nefazadone is rare and should not be completely excluded due to FDA warnings although practitioners should certainly be aware of it. With respect to bipolar disorder there is very little evidence, this is controversial area, and there are certain specialists in the field who feel that those with bipolar disorder should not be put on antidepressants as it may push some into manic episodes. This does not happen regularly but is something to be aware of and the use of a mood stabilizer would reduce the risk of that occurrence. However, most practitioners who treat bipolar patients use antidepressants. Dr. Martin suggests that when the indication of bipolar disorder is discussed antidepressants be made available.
- × Dr. Ballasiotes addresses the subject of determining the pediatric cut-off. He speaks to the adolescent and pre-adolescent population's ability to metabolize drugs more quickly than adults. In respect to nefazadone, those patients who are not only mentally ill but suffer from substance abuse, benefit greatly from this drug, as it allows them to gain quick control of their nervous system. He concludes by saying that he continues to treat people with HIV and HEP C by prescribing nefazadone although he proceeds with caution after the warning of possible liver toxicity.
- × Dr. Mioshi comments on the subject of adherence to the drugs explaining that most side effects of SSRI's are gone within a couple of weeks with the exception of dry mouth. However, drop out rate after one month is at 28%, and after three months, which should be a cut-off, practitioners should be able to communicate to their patients the reasons for the side effects and that most of them they will go away in time.

- Dr. Goo asks Dr. Mioshi and the rest of the panel if there are any clinically relevant drug interactions, specifically with Prozac
- Dr. Mioshi replies that codeine converted to morphine is one specific drug interaction, but that not many people use Tylenol 3 anymore, and that there are a few others.
- Dr. Helfand replies that he is not sure if psychotics are immune to Prozac, but tricyclics, MAO Inhibitors and anti-psychotics, especially older ones can be dangerous with some 2nd Generation Antidepressants, but there are other drugs that can be used. He adds that OHSU did not uncover many potential adverse events.
- An unidentified speaker mentions Warfarin as a problematic drug interaction.
- Dr. Thompson asks for the psychiatric view of first starts, monitoring programs, escalating dosage or switching medications with or without side effects. He explains that he has had similar discussion with DSHS colleagues and would like to know what the committee members or the guest speakers feel is an adequate trial of a first start medication with a patient.
- Dr. Martin explains that it is necessary to treat a patient for 8-12 weeks for any med at a substantial dose before augmenting, switching, or adding another drug. If there is no response after this time with this first drug it would then be necessary try another drug. If there were a response then after this same time period it would be necessary to then try a new dose or some other aforementioned strategy.
- Dr. Lessler asks for discussion from committee before opening the floor to stakeholder input.
- Dr. Bray voices his concerns about making certain drugs therapeutically interchangeable with other drugs, as some groupings are reasonably similar and other are not.
- Dr. Reese states that he concerned about this subject as well and feels that if a practitioner finds an antidepressant that works well with the patient and then the drug is interchanged the therapy may be compromised.
- Dr. Graham explains that he will present a flowchart to the committee that explains the process of preferred and non-preferred antidepressant prescription presented to retail pharmacies. He then defines the word REFILL as “the continuation of therapy with the same drug, including the renewal of previous prescription or adjustment in dosage when a prescription is for antipsychotic, antidepressant, chemotherapy, antiretroviral or immunosuppressive drug.” He further explains that this does not address someone who comes in to program on a drug for a refill, this individual would then need some prior approval, particularly in the Medicaid system.
- Flowchart is displayed on projection screen.
- Dr. Graham directs the committee members through the flowchart explaining the steps; a prescription is submitted to the pharmacist, the computer will ask if it is a preferred drug- if the answer is yes the prescription is then filled. If the answer is No the computer then asks if it is a refill, if the answer is Yes the prescription will be refilled. If the answer is No the computer asks if it was prescribed by an endorsing practitioner, if the answer to that question is Yes and practitioner has written DAW the drug is then filled. If the prescription was submitted by a practitioner who does not endorse the PDL then the standard procedure for a prior approval would be carried out. If the prescription was submitted by an endorsing practitioner who did not write DAW this is the point where the medication will be subject to therapeutic interchange.
- Dr. Bray asks if it is refilled would it have to be by the same provider.
- Dr. Graham replies that it would not matter as the drug history is in system.
- Dr. Reese asks what the consequences would be if the patient were to transfer from another insurance.
- Dr. Graham explains that in such a case the system would not recognize it.
- Dr. Reese raises the concern of a therapeutically interchanged drug in this particular class and that a situation in which an endorsing provider may not sign DAW is a possibility.
- Dr. Graham replies that the practitioners must understand the system in order to make this work and he believes people are beginning to learn the program.
- Dr. Goo inquires as to the patient transferring from a different insurance plan and if it would be a possibility to expedite drugs for those patients who have been on the drug for some time or if they would have to contact their insurance plan.
- Dr. Graham replies that this would be something to work out administratively within programs.
- Dr. Thompson comments that it would be no different from a standard transfer to a new health plan at the beginning of the year, any documentation showing that it is a continuation of therapy will be honored.
- Dr. Lessler asks for other comments.
- Dr. Goo asks if there is any comment on the data coming from Europe regarding the overdose death potential with venlafaxine.
- Dr. Mioshi explains that there has been some data that has come from Europe that indicates the cause as being a function of norepinephrine or and SSRI
- Steve Mitchell, psychiatrist, explains that in England only psychiatrists can prescribe venlafaxine, and that the study is not the same across the board and probably reserved for more severely depressed patients.

- × Dr. Ballasiotes comments that there is information from the UK Office of National Statistics showing venlafaxine is involved in a higher rate of deaths from overdose than are SSRI's.
- × Dr. Lessler opens the floor to stakeholder comments on 2nd Generation Antidepressants.

Stakeholder Input

Dr. Lessler asks that the stakeholders keep comments to three minutes or less and that they identify any sponsors and submit all evidence to OHSU

- × Dr. Bill Schmidt of GlaxoSmithKline, Medical Affairs comments that the OHSU EPC report is important for both what it says and what it does not say, explaining that the report concluded that the efficacy and effectiveness of these drugs is similar although it does state that they are not identical. The report does offer that side effects profiles are quite a bit different from each other, which is very important as side effects are a critical factor in patient compliance. He does state that the report did not address long-term concerns regarding differences between the drugs as far as adherence. Since efficacy and tolerability are critical to long term adherence, a controlled release formulation of paroxetine was developed with the goal of reducing side effects a few years ago. This formulation, which is marketed as Paxil CR, is unique among the SSRI's as it bypasses the stomach and is absorbed over four to five hours in the GI tract. The improved pharmacokinetic profile does yield significantly lower rates of nausea and vomiting compared with the immediate release SSRI's and pooled adverse event dropout rates were similar to placebo in depression trials. Based on the results from a managed care depression database study published in 2003, Paxil CR was associated with a 28% lower risk of early discontinuation compared with immediate release SSRI's which include paroxetine IR, and results are shown graphically on this visual. (Colleague displays graph) The top line shows a greater percentage of patients actually remaining on therapy while on the controlled release form than with all comparative drugs. A subsequent economic analysis of these same results demonstrated that the controlled release paroxetine was associated with lower overall medical costs compared with the immediate release form of paroxetine. To answer all clinical needs spoken of throughout the meeting the controlled release formulation of paroxetine has been shown to offer efficacy along with improved tolerability that can lead to improved compliance. Those clinical advantages are complemented by a potentially fallible economic profile that GlaxoSmithKline feels makes Paxil CR a desirable evidence based choice for formulary inclusion.
- × Barry Patel of Wyeth Global Medical Affairs, comments that there is a good understanding norepinephrine and serotonin and which patients need to be treated with which medication first. In that regards, in a product that inhibits uptake the hypothesis considers efficacy in terms of remission. There are head-to-head studies that signal various meta analyses with significant overlap. There are products studied for a variety of disorders, from anxiety to mood disorders. When studies were done on the SNRI venlafaxine studies show that this was the only one that had depression indications as well as anxiety indication, unique in indication. The United Kingdom has asked Wyeth to change labels in the IK only stating that the SNRI- venlafaxine is unique in its indication, this also addresses the earlier question regarding Europe. Wyeth's website provides a Q and A, which addresses all risks and benefits of product.
- × Dr. Steve Mitchell a Seattle psychiatrist, comments on the significant factor in psychological as well as medical well being of individuals of this state. He raises three points;

    1. Most clinicians know that antidepressants effectiveness and efficacy are similar and not identical, it is also known that side effect profiles among the drugs buproprion and Wellbutrin have less sexual and weight side effects when compared with the SSRI's. Another factor is that compliance and longer-term adherence to therapy which have also been tied to dosing regimens. Unfortunately, the clinical usefulness of a drug, even one with a desirable side effect profile can become significantly diminished if the drug must be taken two or three times a day, Medicaid patients in particular cannot afford treatment failures because of poor compliance.
    2. Many patients benefit from the efficacy and favorable side effects of Wellbutrin, until recently Wellbutrin had to be taken at least twice daily and a significant portion of patients forget to take their afternoon dose on time, missed doses can reduce efficacy and second doses taken too late in the day can increase undesirable side effects such as insomnia. The end result can be a poor outcome in needless exacerbation of symptoms as well as wasted time and money. For example, the per capita health care cost in this country is over $5,000 a year now, Wellbutrin recently became available in a once daily formulation, Wellbutrin XL, this new formulation eliminates multiple daily dosing, rapid increases and decreases in buproprion plasma levels are significantly

reduced, thus compliance improves and some side effects are reduced. Increased compliance can result in better outcomes, which can translate into fewer office visits, less switching, and augmentation, and less time and money wasted. Wellbutrin XL answers major clinical needs handling major compliance through once daily dosing as well as potentially improved side effect profiles. This is a favorable choice for formulary inclusion.

× James Addams, a representative for NAMI Washington, has had fifty years of experience with family members with depression and a suicide. Individual patients with the same diagnoses have different responses to medications which effects compliance with treatment. Side effects are a great influence on compliance and there needs to be a greater menu of options as a person grows older. There is limited evidence showing a debilitating effect that occurs over time in a person taking the same medication for extended periods. His concern is that studies do not include medication costs; the medications included on formulary should have the least amount of risk to getting optimal treatment for the disease. He also comments that at some point there must be someone identified as the person responsible for damage caused.

× Dr. Dan Wanwig, psychiatrist and internist in Tacoma, had experience with seriously disturbed patients and feels strongly that sertraline should be included on the recommended list. Hew explains that there are two reasons for his recommendation of sertraline. The first reason is that this drug has the widest spectrum of indications by the FDA; includes not only major depression but social anxiety disorder, panic disorder, post traumatic stress disorder, Obsessive Compulsive Disorder and Premenstrual Dysphoric Disorder. Real world consideration- Many of the patients excluded from studies cited were excluded because they had a heavy loading of co-morbidities. Most patients these days seen by psychiatrists and mental health professionals have co-morbidities, not only mental but medical. He uses sertraline with depression, personality disorders, and dementia associated with Alzheimer's. Sertraline works safely in those who have had myocardial infarction and angina, sertraline has an intermediate elimination half-life. He strongly recommends that sertraline be placed on the formulary.

× Dr. Amir Karmazidia, senior scientist with Forest Laboratories, comments that little information was presented about escitalopram. The goal of any clinician is to improve outcome in patients, the way to do that is by improving compliance. It is necessary to find a drug with equal or better efficacy in its drug class, a safe drug as well as one that is easy to build. Lexapro has many similarities within its class as far as efficacy, however, with Lexapro symptom improvement happens as early as week one or two; this has not been seen with other SSRI's. As far as safety, geriatric pts and drug-drug interaction, Lexapro has the least propensity for drug-drug interaction to mediate it by Cytochrome P450, also, it has the least protein binding at 56%, with no drug interaction, and this makes Lexapro the cleanest SSRI available. It has the narrowest dose range, so that if there is need to tartrate a patient, the does would only go up or down one step that improves compliance significantly in patients. One of the only two drugs in the SSRI category that has the GAD indication also found an SNDA for panic and Social Anxiety Disorder.

× Dr. Larry Cohen, Psychiatric Pharmacist with 26 years of experience working with psychiatric patients, announces that he will not be speaking in the defense of any one pharmaceutical because he feels that all the drugs in this class have value and should be available. He comments that there were few quality head-to-head outcome studies and it is important that a review be done on consumers in this state by people who are involved in providing care. This review should involve the outcome definition of refills and decisions limiting the agents used, this would be an opportunity to evaluate the impact of this in Washington State. If, There can be problems associated with a definition that is put in place requiring a Dispense As Written and its impact should be studied in detail. There needs to be open access to a broad based armamentarium. He supports the use of generics, the only qualifier being that every effort should be made to treat the patient with the same generic manufacturer product, which may have to be done on a local level. As much as is known about the SSRI's there is not enough information to understand why an individual patient responds to one SSRI and not to another. Patients are different and it is important to find the best drug for each individual. It is also true that a patient may not respond to a single agent and that multiple antidepressants must be used for a specific patient, this is not a general rule, but when it is achieved, understanding the history and identifying that this is necessary is something that needs to be available to providers. In respect to patients suffering from depression, bipolar disorder, schizophrenia, as well as other disorders, those who do not reach full remission are at risk of becoming refractory to treatment and having episodes more frequently. Treatment adherence will help to lessen the amount of patients who require in hospital care. He wants to know what will happen if there are policies in place that require people be changed to another medication. He states that it is important that the patient be tried on that medication again unless they have had an adverse event. If patients are obligated to switch medications he would like to know how that will be funded. He feels it is important to look at that outcome data, not just evidence based medicine reviews studying the head-to-head trials which are limited in the literature in terms of treating depression.

- Dr. Sharon Romm, associate professor of psychiatry at the University of Washington speaks on behalf of Pfizer. She comments that sertraline should be on preferred drug list explaining that she treats a large number of severely depressed patients both in and out of hospital. The antidepressant should be chosen by the doctor, each patient is unique, and physicians need to do what is best based on their professional opinion of excellent care. She takes issue with the OHSU report, believing the review to be biased. 70% of the randomized controlled trials of the SSRI's were omitted, stating that all SSRI's are equivalent but neglecting to define what equivalent means, the reports are not assembled by specialists nor endorsed by the Oregon State University Department of Psychiatry. No data supports using these reports to show improved outcome or money saved. Cost is considered but reviewers neglect such important issues such as weight gain and withdrawal symptoms after stopping the medicine. These are problems that only add to the patients' misery on top of their depression. As an example, she offers studies showing that paroxetine treated patients gain weight and report significant adverse events on interruption of treatment as compared with those treated with sertraline. Sertraline has consistently been associated with lower total treatment costs and depression. The reviewer neglects to look at how patients' lives improve when the illness is adequately treated, it does not include that doctors have the privilege to observe in daily care that when patients get better, relationships flourish, housing and employment stabilizes and lives improve. The review also neglects how specific patient populations respond and neglects drug-drug interactions. She gives the example that the reviewers neglected to acknowledge the sertaline antidepressant heart attack randomized trial study that addressed safety in using sertraline in patients' post-MI and with unstable angina. Depression worsens ultimate prognosis of these conditions. This information has been added to the package insert so physicians now prescribe sertraline with increased confidence. Medically compromised patients are put on multiple medications, a drug is needed that can be used with assurance that there will be no interaction with whatever else the patient takes. Sertraline has a low propensity for drug-drug interaction with less inhibitory affect on Cytochrome 2D6 and some other SSRI's. Reviewers neglect to consider that sertraline has the most short and long-term indications for mood and anxiety disorders including panic, Post Traumatic Stress Disorder (PTSD) and Obsessive Compulsive Disorder (OCD). Sertraline significantly decreases the risk of relapse of depression and PTSD in 52 week studies and Panic Disorder and OCD in 80 week studies. Prescribing the cheaper SSRI's without FDA approval for these multiple indications is essentially using them outside of their label, which is not the intent of the FDA. The evidence in evidence based medicine is with sertraline. She urges the committee not to lose sight of the litigious nature of society, not to risk prescribing a drug without FDA approval. The bottom line is that choosing a drug based on cost alone is bad medicine. She concludes by saying that mental health is different from other medical specialties, patients are unique and so is their response to the medicines prescribed. There is a plea made to have access to all available drugs so that the best medicine can be practiced, and this armamentarium needs to include Zoloft.
- Lenora Warden, a consumer, comments on her experiences with Celexa. She says that she owes her life to this drug. She has spent fourteen of the last twenty-four years in the hospital trying to figure out which drug worked for her. Nothing worked because the clinician did not listen to her, she was homeless for four and half years and no one understood that she did not want to be homeless. She was unable to get medical coupons because she would forget how to make an appointment, once she did get the coupons she realized that the state did have an interest in helping people like her. She says that patients must be included in the process. Clinicians often say that a specific drug is good for a patient but they do not often listen to what the patient needs. The clinicians do not always seem to understand the way it feels to live with this disease, they do not seem to understand how it feels to be unable to dress yourself, or forget who you are entirely. If Celexa is not available she explains that she would go through withdrawal and her version of withdrawal is to suddenly find herself with no identity. She explains that she may be capable of walking off a bridge, that she takes no responsibility for her actions. She implores that the clinicians understand their patients and keep Celexa on the formulary to keep her and people like her out of the hospital.
- Dr. Roger Jackson, Chief of Medical Staff at Western State Hospital, says that in his 25 years of practice he has always worked on inpatient settings. He comments that the good news is that the fraction of the population in the hospital receiving treatment for depression has decreased rapidly since his residency in 1978. This shows that the treatments have been working. With regard to his experience at Western State Hospital, their drug use guidelines already have prescriptions against the use of therapeutic duplication for SSRI or antidepressant agents in general without clinical director approval. He has also been involved in a group that intends to bring proposal in front to the P&T Committee and the hospital at Western State is supportive of the proposal being made by MAA. Patients all respond differently to various kinds of medications, although, most of the SSRI's are very similar to one another, in respects to beginning treatment. He asks how important is it to have all drugs available when clinicians can select drugs based on side effects and possible drug-drug interactions with other treatments. When considering ongoing treatment over the course of an illness it is important to have a broad range of drugs from which to draw.

- Katie Tomaser, pharmacy director of Western State Hospital, speaks for the mental health division of DSHS. She agrees with previous speakers that patients are different and medications do not react the same with each patient, however, she does not believe that very unrestricted access to every antidepressant on the market is necessary. The Mental Health Division of DSHS supports Medicaid's initiatives to develop a formulary for antidepressant and to develop the mental health initiative.
- Dr. June Braden, a family physician representing the division of developmental disabilities within DSHS, practiced full time with developmental disabilities for seven years, is the medical director of a long-term residential autism center in Bremerton, and works part time at Rainier School. She explains that she has been involved in Dr. Thompson's discussions about mental health drugs and formularies and access. As part of her job at Morgan Center, she is involved in doing respite care for up to one hundred adolescents and young adults afflicted with the most challenging autism and related psychiatric disorders in the state. She also supports the MAA initiative; in fact, Rainier School and Morgan Center have essentially established the same policy voluntarily within the physicians group. A decision was made about two yrs ago, as SSRI's are very similar in respect to response rate, to try a limited number of drugs first and to keep an open formulary for those patients who do not respond to a first drug. Her clients have done well with this process and she believes that she represents a group of clients that are more medically fragile and have higher rates of seizure disorders and concomital medical illnesses than any other practice on the state. Over 60% of her patients have significant seizure disorders, many of them have multiple genetic anomalies, and even in that population the use of Prozac and Paxil generic first has been very safe and effective. She explain that the best way to distribute resources without compromising client care would be to provide financially the best access to all drugs to the most people.
- Eleanor Owen, citizen advocate for 25 years, voices her concerns about the general response to SSRI's from individuals who are given the drugs, she explains that the response has repeatedly been that they feel they have had little or no impact on the selection of their medication, numerous patients tell her that the drugs they are taking do not work for them and yet the clinicians continue to prescribe this medication. She comments that she would like to see research studying the comparing those individuals on multiple drugs with those on a single drug. She feels that there are now enough resources to track what does and does not work for each patient. She asks that the practitioners listen to what the patient has to say, they do know how their drugs interact with their bodies.
- Representative Bill Hinckle of the 13th legislative district, a long-standing advocate of mental healthcare, comments that he has seen people in crisis and has seen what has worked and what has not worked, he has witnessed patients complaining that their drugs were switched and that the switch is not working. He appeals to the committee to give practitioners the widest berth possible in respect to drug selection. Because, not only are the mentally ill a delicate population, they have an impact throughout the system, particularly in respects to state costs. If advantages are taken away it impacts, juvenile and adult justice systems and the costs are exorbitant, he implores the committee to consider this aspect before moving forward with a motion.
- Dr. Lessler asks for further comments from stakeholders or committee members. After receiving no response he concludes the P&T Committee and announces that the deliberation for the motion of the Second Generation Antidepressant drug class will be continued at the next meeting.
- Dr. Graham announces that the next meeting will be the third Wednesday in February.

2:30 Meeting adjourned.

DUR Board Meeting Minutes
December 15, 2004

WASHINGTON STATE PHARMACY AND THERAPEUTICS COMMITTEE MEETING
Regular Meeting
Radisson Hotel SeaTac

2:00pm – 4:00pm

Council Members Attending: Alvin Goo, Pharm D, Patti Varley, ARNP, Carol Cordy, MD, Dan Lessler, MD, Robert Bray, MD, T. Vyn Reese, Angelo Ballasiotes, Pharm D., Jason Iltz, Pharm D., and Janet Kelly, Pharm D. John White, PA, was absent.

Medical Assistance Administration, Coordinating Staff: Jeff Thompson, MD, MAA Chief Medical Officer; Joan Baumgartner, MD, MAA Medical Consultant; Siri Childs, Pharm D, Pharmacy Policy Manager; MAA, Nicole Nguyen, Pharm D, Clinical Staff Pharmacist, MAA; and Carolyn Grimm, Secretary Admin, MAA

Observers: Calvin Harris, Forest; Slater Sparks, Bertek; Olga Villalpando, GSK; Don Stecher, Novartis; Katy Tomisser, PharmD, Western State Hospital; and Elizabeth James, Pharm D.

I. ADMINISTRATIVE ITEMS

The meeting was brought to order by Chairman, Dan Lessler, MD. The minutes of the previous DUR Board Meeting on September 15, 2004 were approved. The members of the Washington DUR Board introduced themselves.

II. "A CLINICALLY SOUND APPPROACH TO MEDICAID COST CONTAINMENT – PSYCHOTHERAPEUTICS"

Jeff Thompson, MD, introduced Annette Hanson, MD, former Massachusetts Medicaid Medical Director, who gave a presentation entitled, "A Clinically Sound Approach to Medicaid Cost Containment – Psychotherapeutics". (See attached) Dr. Hanson's presentation covered the following:

- MassHealth Overview – FY 2004 Actual pharmacy expenditures were less than Projected budget and less than FY 2003
- MassHealth Overview – FY 2005 Projected budget
- MassHealth Cost Drivers – Pharmacy expenditures were rising the fastest of all cost drivers in Massachusetts Medicaid
- Management of Psychotropic Medications resulted in significant cost savings without sacrificing clinician autonomy and patient access to medication
- Focus on Evidence-based treatments for mental health
- Focus on Physician education: "Dear Doctor Letters"
- Polypharmacy initiative resulted in significant cost-savings and improved patient care (Duplicate 2nd generation antidepressants, duplicate atypical antipsychotics, and more than 5 mental health drugs concurrently)
- For 2nd generation antidepressants: generic drug first on all new starts and PA on therapeutic duplication
- For Anticonvulsants/mood stabilizers: PA required for Neurontin, Keppra, Topamax, and Gabitril
- For atypical antipsychotics: PA for therapeutic duplication
- Results: cost-avoidance was $11.9 million for antidepressant initiatives and cost-stabilization/cost-avoidance for the atypical antidepressant initiative was $175,048.

Dr. Hanson stressed the importance of involving stakeholders to help plan and develop the "best practices" in delivering appropriate mental health drug therapy in the Medicaid population. Her goal was to "reduce Medicaid pharmacy expenditures while preserving clinician autonomy and patient access to medication as much as possible". She put together a clinical workgroup of mental health experts and other medical experts that took care of mentally ill Medicaid clients. These experts recommended the drug initiatives that eventually were implemented in Massachusetts. Some of the workgroup members volunteered to act as consultants on behalf of the Medicaid drug initiatives to help other providers "buy-in" to the program. Dr. Hanson attributes the success of the program to the dedicated work of these experts and the active participation of stakeholders.

Other important factors leading to the success of the program were the following:

- "grandfathering" all existing prescriptions
- "stable" (not hospitalized in the last six months) patients not required to change
- Inpatient units were asked to get any prior authorizations as part of discharge plan
- "new" starts were asked to use generic first; adequate dosage and length of trial were required before a change to a different medication (unless adverse event).

Dr. Hanson concluded her presentation and responded to questions from the DUR Board members and stakeholders. The following text has been transcribed from a recorded tape at the meeting:

Questions and Answers from the P& T Meeting
December 15, 2004
Dr. Annette Hanson

Q. "Going back to the mailers that went out initially for prescribers who had patients who were on large numbers of Meds and the effectiveness of that…. My observation would be that everything that I have read in health services would suggest that there is no way that should have worked and yet clearly it did. I'm just curious and if you could comment more on why you thought mailing out a series of letters in that way would change prescribing habit."

A. "I think it was a combination. 1) The letters went to individual doctors with a list of their patients and so it was not just a generic mailing. It was a personalized letter. 2) more important then that, we had all this media education, everybody knew about it. The Psychiatric society had a letter in their monthly mailing and their newsletter about it. It had been in all the newspapers, it had been on the radio, just everybody knew about it. And then we met with people and had these educational endeavors. I said to the workgroup that you each need to go and talk to the constituents you're here representing. You need to be helping them to understand this and the severity of it and that we don't have any money and these are not good practices. This is just plain not good medicine and we need to really try and do better. And somehow that message got out. We also sent out little blurbs when they got their reimbursement checks that said "Don't forget the MassHealth Drug List". In retrospect, it was not fun but it was not a bad thing. It was a coming together. The community had been working on this for a couple of years and working on "Best Practices"."

Q. "Your comment about getting a broader understanding that there are trade offs for opportunity costs in economic terms if you do this over here that you allow whatever atypical to be prescribed and however many and so forth. And then your not going to do this i.e. provide breath of coverage for a population. I was wondering, and it sounds like you got that message out to the medical community and some how you referred to that, I was wondering if there was anything you did that was particularly effective along those lines and along those same lines you mentioned that the state did go back and put 40,000 people who had lost benefits somehow regained benefits."

A. "A couple of things I did 1) I'd been pretty active in the medical society and my medical society has public payer workgroups and I used to go to that a lot. So I knew those people already. These are the people who knew the difference between Medicaid and Medicare, which is not true for everybody. They were really very helpful and they also had letters in the "Vital Signs" which is the monthly newsletter for the Mass Medical Society around these kinds of issues. That was helpful. I called up people at the hospitals and I told them that I just needed their help. Another thing that I said to the Doc's was, we don't pay you enough for what you do for our Medicaid clients because I don't have any money to pay you more. The next year there was a 5% increase of pay for the Doctor's because of this."

Q. "I apologize if this question was asked and I missed it….. I would imagine that one of the arguments that naysayers would have been saying is that when you squeeze in one place it pops up somewhere else…. for example reduced medications, may make hospital admission go up, suicide death may go up, I imagine you looked at that?"

A. "We did. As a matter of fact, I told you that I like to do evaluations, so we set up a program where the University of Massachusetts and the University of Maryland are doing evaluations of this entire endeavor and we do it by the drug class. The drug has to be on the list for a year because with the grandfathering it wouldn't be totally in place for a whole year. We have done three classes so far, we've done the NSAIDS, PPIs and anti-histamines. They have other that they are doing. There hasn't been any increase in hospitalization. You have do it by diagnostic category you can't just look at across the board…so you have to look at psychiatric patients and even by age category to see whether or not there was a difference in hospitalizations and so on and so far we have not had any increase. Even looking at total admissions and there was not an increase."

Q. "As a primary care physician/family doctor...I develop a spontaneous movement disorder when I realize that my specialty colleagues can prescribe something and I can't. I have to jump through a lot of hoops to get there. I am thinking about the anti-seizure drugs and so I'm wondering what the response was from primary care physicians to that ruling and the other side of the coin is that is sets up access problem if people don't have access to specialty care."

A. "If you write "for seizures" on it and the patient has a history of first line seizures medications, it will go through the computer system without a stop. The whole system looks at two things: 1) Does it say seizure disorder and 2) if you're a neurologist you go through…..and 3) if the patient is on another first line anticonvulsant. Now guess what? I had a psychiatrist write "for seizures" on the prescription, so we looked up the case, the patient didn't have seizures, guess what happened to that guy….we sent him to fraud and abuse. We have it to where you have to be a specialist. The other thing (which I didn't talk about) there are not enough child folk and there never will be and I finally gave up on thinking we could train enough to be adequate and so pediatricians are going to be doing the bulk of the prescribing and family practice doctor's for children with psychiatric disabilities."

III. DRUG UTILIZATION REVIEW

MAA calculates that 2nd generation antidepressants and atypical antipsychotics represent more than 20% of Washington Medicaid's drug expenditures.

IV. MANUFACTURERS' PRESENTATION

There were no manufacturers' presentations to the DUR Board during the meeting. Please refer to the December 15, 2004 Pharmacy and Therapeutics Committee meeting minutes (same day) for comments related to the Medicaid Mental Health Initiatives.

V. STAKEHOLDERS' PRESENTATIONS

There were no stakeholder's presentations to the DUR Board drug the meeting. Please refer to the December 15, 2004 Pharmacy and Therapeutics Committee meeting minutes (same day) for comments related to the Medicaid Mental Health Initiatives.

VI. RECOMMENDATIONS OF COUNCIL

- Dr. Dan Lessler asked MAA to submit a proposal to the DUR Board at the next scheduled meeting that would be a comprehensive package outlining all the components of the Mental Health Drug Initiatives, complete with implementation processes and timelines.
- Dr. Lessler stated that he and other DUR Board members would like to participate in a subcommittee/ workgroup to help plan the design and implementation of the Mental Health Initiatives to be brought back to the next DUR Board meeting.

ADJOURNMENT

The meeting adjourned at 4:00pm